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Biotechnology

Did the coronavirus leak from a lab? These scientists say we shouldn't rule it out.

For many scientists, challenging the idea that SARS-CoV-2 has natural origins is seen as career suicide. But a vocal few say it shouldn't be disregarded or lumped in with conspiracy theories.

by **Charles Schmidt**

March 18, 2021



THE YOMIURI SHIMBUN VIA AP IMAGES

Nikolai Petrovsky scrolling through social media



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chairman of a company called Vaxine that develops immunizations for infectious diseases, among other projects. Since 2005, he's received tens of millions of dollars in funding from the US National Institutes of Health to support the development of vaccines and compounds called adjuvants that boost their effects. After Chinese scientists posted a draft genome of the novel coronavirus SARS-CoV-2, the disease culprit in Wuhan, Petrovsky—who by this time had put skiing on the back burner to work from his Colorado home office—directed his colleagues down under to run computer modeling studies of the viral sequence, a first step toward designing a vaccine.

This generated a startling result: the spike proteins studding SARS-CoV-2 bound more tightly to their human cell receptor, a protein called ACE2, than target receptors on any other species evaluated. In other words, SARS-CoV-2 was surprisingly well adapted to its human prey, which is unusual for a newly emerging pathogen. “Holy shit, that’s really weird,” Petrovsky recalls thinking.



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As Petrovsky considered whether SARS-CoV-2 might have emerged in lab cultures with human cells, or cells engineered to express the human ACE2 protein, a letter penned by 27 scientists appeared suddenly on February 19 in the prestigious medical journal The Lancet. The authors insisted that SARS-CoV-2 had a natural origin, and they condemned any alternate hypotheses as conspiracy theories that create only “fear, rumors, and prejudice.”

Petrovsky says he found the letter infuriating. Conspiracy theorists is “the last thing we were,” he says, “and it looked to be pointing at people like us.”



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Last month, a team of international scientists completed a month-long visit to Wuhan to investigate SARS-CoV-2's origins. Convened by the WHO, and closely monitored by Chinese authorities, the team concluded initially that a lab leak was so unlikely that further investigations of it were unnecessary. The WHO's director general later walked that statement back, claiming that "all hypotheses remain open and require further analysis and studies." A group of 26 scientists, social scientists, and science communicators—Petrovksy among them—have now signed their own letter arguing that WHO investigators lacked "the mandate, the independence, or the necessary accesses" to determine whether or not SARS-CoV-2 could have been the result of a laboratory incident.

The WHO investigation follows a year during which debates over SARS-CoV-2's origins turned increasingly acrimonious. Chinese officials were, and still are, unwilling to provide information that might settle lingering questions about where the virus came from, and in the absence of critical data, expert views coalesced around two competing scenarios: one that a lab leak was plausible and needed more scrutiny, and another that SARS-CoV-2 had almost certainly spilled over from nature and that the odds of a lab leak were so remote that the possibility could essentially be taken off the table. Those insisting on a natural origin say the virus lacks genetic features that would show it to have been deliberately engineered. But it's also possible that



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the pandemic began, and with then-president Trump fuming about a “Chinese virus,” many scientists and reporters became “cautious about saying anything that might justify the rhetoric of his administration,” says Jamie Metzl, a senior fellow at the Washington, DC–based Atlantic Council, an international affairs think tank.

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It could have been career suicide for scientists to voice suspicions about a possible lab leak, says Metzl, especially when there was already a long history of viral disease outbreaks spilling over from nature. Alina Chan, a postdoctoral fellow specializing in gene therapy and cell engineering at the Broad Institute in Cambridge, Massachusetts, echoes that view. Chan says the risk of challenging the orthodoxy that SARS-CoV-2 has natural origins—an entirely plausible hypothesis, she maintains—is greatest for established scientists in infectious disease with supervisory roles and staffs to support. She herself has spent much of the last year calling for more scrutiny of a potential lab leak, claiming that as a postdoc, she has less to lose.

The vitriol also obscures a broader imperative, Relman says, which is that uncovering the virus’s origins is crucial to stopping the next pandemic. Threats from both lab accidents

and natural spillovers are growing simultaneously as humans move steadily into wild places and new biosafety labs grow in number around the world. “This is why the origins question is so important,” Relman says.

“We need a much better sense about where to place our resources and effort,” he adds. And if a lab release for SARS-CoV-2 looks plausible, Relman says, “then it absolutely deserves a whole lot more attention.”

If SARS-CoV-2 did spill over into humans from the wild, how and where did that happen? A year into the pandemic, these remain open questions. Scientists still speculate about whether the virus passed directly into humans from infected bats (known reservoirs for hundreds of different coronaviruses) or through an intermediary animal species. The Huanan Seafood



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A lab-escaped virus, meanwhile, would have been introduced to the world by a researcher or technician who became infected with it. These sorts of lab leaks have happened before, and were implicated in several cases of community transmission during SARS outbreaks in the early 2000s. In 2017, the Wuhan Institute of Virology became the first lab in mainland China to receive a Biosafety Level 4 (BSL-4) designation, the highest security status for a research space. But the institute also has a history of questionable safety practices. The lab's scientists reported a lack of appropriately trained technicians and investigators at the facility, prompting US diplomatic scientists who visited in 2017 and 2018 to alert the State Department. At the same time, many scientists have pointed out, particularly in the aftermath of a recent, and for some, contentious, examination of the lab-leak hypothesis in New York magazine, that coronaviruses have typically been handled at BSL-2 or BSL-3—lower security levels.

Such caveats aside, a prevailing theory among lab-leak proponents has been that SARS-CoV-2 was not simply brought into the Wuhan lab but was somehow engineered there, given that many of its scientists routinely perform genetic research on coronaviruses and may also have “collaborated on publications and secret projects with China’s military,” according to a US State Department fact sheet released during the last week of the Trump administration. On March 9, a Washington Post columnist, citing an unnamed State Department official, suggested that the Biden administration—while stopping well short of endorsing any particular theory regarding the origin of the virus—did not dispute many of the points made in that fact sheet.

Still, skeptics who doubt the lab-leak hypothesis say SARS-CoV-2 doesn't look anything like an engineered virus. Instead of appearing in discrete chunks, as would be expected with a genetically engineered microbe, the differences with RaTg13 are distributed randomly throughout the viral genome. In an email to Undark, University of Chicago emeritus virology professor Bernard Roizman wrote that “we are many, many years away from a complete understanding of viral gene functions and regulation—the key elements critical for construction of lethal viruses.”



The virus does have an inexplicable feature: a so-called “furin cleavage site” in the spike protein that helps SARS-CoV-2 pry its way into human cells. While such sites are present in some coronaviruses, they haven't been found in any of SARS-CoV-2's closest known relatives. “We don't know where the furin site came from,” says Susan Weiss, a microbiologist who co-directs the Penn Center for Research on Coronaviruses and Other Emerging Pathogens at the



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Stanford microbiologist David Relman believes the lab-leak hypothesis was never given a fair hearing.

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Relman says it's also possible that scientists working with undisclosed and even more closely related coronaviruses—perhaps one with a furin cleavage site and another with the SARS-CoV-2 gene backbone—may have been tempted to create a recombinant virus so they could study its properties. Indeed, researchers at the Wuhan Institute of Virology initially failed to disclose that eight other SARS-like coronaviruses had been detected in samples collected from the same mine cave where RaTG13 was found. Workers who cleaned bat feces in that cave, located in Yunnan Province near the border with Laos, went on to develop severe respiratory disease, and one of them died.

Petrovsky leans towards another potential scenario, namely that SARS-CoV-2 might be evolved from coronaviruses that snuck into lab cultures. Related viruses in the same culture, he ✕ explains, such as one optimized for human ACE2 binding and another not, can swap genetic material to create new strains. “We’ve had this sort of thing happen in our own lab,” he says. “One day, you’re culturing flu, and then one day you sequence it, and you go, ‘Holy shit, where did this other virus come from in our culture?’ Viruses are evolving the whole time, and it’s easy for a virus to get into your culture without you knowing it.” Petrovsky and several coauthors speculated in a paper published as a non-peer-reviewed preprint in May of last year



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BioRxiv staff replied that it would be more appropriately distributed after peer review, “which stunned us,” Petrovsky says. “We thought the whole point of preprint was to get important information out quickly.”

The paper was subsequently posted on a different preprint server called arXiv.org, based out of Cornell University. Soon reporters came calling, but most were from right-wing news outlets representing what Petrovsky calls “the Murdoch press.” Petrovsky says he had to work at stopping some tendentious reporters from distorting his paper’s findings to shape a narrative that SARS-CoV-2 had unequivocally been manufactured. And at the same time, he says, other media tried “to make a mockery of the whole possibility of the lab thing.”



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Petrovsky describes himself as politically neutral, and according to sources, he is highly regarded in the vaccine world. Maria Elena Bottazzi, a microbiologist at Baylor College of Medicine, in Houston, says Petrovsky doesn’t make scientific claims that aren’t fully supported by evidence. And yet, simply following the science, Petrovsky suggests, had become too politically fraught. They were “dealing with global forces,” he says, “that are way more powerful than a scientist trying to tell a science-based story.”

The Australian findings were also caught up in a backlash against papers claiming evidence of lab origins by scientists who had jumped opportunistically into the field. Many of these scientists had little relevant experience and no understanding of “how molecular evolution actually works,” says Rasmus Nielsen, an evolutionary biologist and coronavirus expert at the University of California, Berkeley. X

Nielsen cites as one example a JanuRY 31 paper posted on bioRxiv by researchers from the Indian Institute of Technology, in New Delhi, that suggested there was an “uncanny similarity” between aspects of SARS-CoV-2 and HIV. In response to a deluge of criticism, the authors



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the time and resources to do.”

By late spring of 2020, scientists in the natural-origins camp had taken the upper hand in shaping opinions. Only a few researchers have looked deeply into SARS-CoV-2’s origins, and according to the Broad Institute’s Chan, the vast majority of those who did not investigate the question simply accepted what they perceived to be the prevailing view. If scientists were unwilling to challenge the orthodoxy for fear of the consequences, Metzl adds, then that “made it hard for journalists to write credible stories about origins, particularly in the absence of evidence.”

Perhaps no one played a greater role in galvanizing scientific opinions in support of natural origins than Peter Daszak, president of EcoHealth Alliance, a New York-based environmental health nonprofit. A longtime Wuhan Institute of Virology collaborator, Daszak—who, in what many sources described as a conflict of interest, was a member of the WHO-led team that visited China earlier this year—received grant funding from the National Institutes of Health to collaborate on research at the Chinese lab. (The Trump administration abruptly cut off this funding in April 2020, but it was later reinstated with new restrictions.) Daszak is purported to have written a first draft of the Lancet statement condemning hypotheses other than natural origins as conspiracy theories. After repeated requests for an interview, the EcoHealth Alliance and Daszak declined to comment for this story.

Stanley Perlman, a microbiologist and professor at the University of Iowa, in Iowa City, is listed as a coauthor of the statement. In an email to Undark, he wrote that the lab-leak idea “has several aspects, ranging from the statement that the virus was designed in a lab to ones that state the virus leaked from a laboratory but was not engineered.” The Lancet piece, he says, focused more on engineering, which “would presumably be for a nefarious reason, but fortunately is impossible with our present knowledge.” The actual text of the Lancet statement, however, never makes this distinction. 

Charles Calisher, an emeritus professor in the Department of Microbiology, Immunology, and Pathology at Colorado State University, is also listed as a coauthor. He says the conspiracy-theory phrase was, in his opinion, over the top. “Unfortunately for me, [Daszak] listed everyone alphabetically, and I was first,” he says. With his phone constantly ringing, Calisher says, he told people he couldn’t say much until more information is available.



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First he held a superspreader event. Then he recommended fake cures.

After dozens of people caught the coronavirus at his expensive conference, tech mogul Peter Diamandis offered fraudulent covid-19 treatments to them, from injectable peptides to amniotic fluid.

piece in the Proceedings of the National Academy of Sciences claiming that a lab origin was among several potential scenarios; that conflicts of interest among those on all sides of the issue had to be revealed and addressed; and that uncovering SARS-CoV-2's true origins was essential for preventing another pandemic. Efforts to investigate the origins, he wrote, "have become mired in politics, poorly supported assumptions and assertions, and incomplete information."

One of the first media calls after the opinion piece was published came from Laura Ingraham at Fox News, Relman says. He declined the interview.

When asked why he thought Daszak and others pushed so strongly against the possibility of a lab leak, Relman says they may have wanted to deflect perceptions of their work as endangering humankind. With so-called "gain of function" experiments, for instance, scientists genetically manipulate viruses to probe their evolution—sometimes in ways that boost virulence or transmissibility. This sort of research can reveal targets for drugs and vaccines for viral diseases, including covid-19, and was used at the Wuhan Institute of Virology in studies showing that certain bat coronaviruses were just a few mutations away from being able to bind to human ACE2. A [2015 paper](#) in Nature Medicine notes that the "potential to prepare for and mitigate future outbreaks must be weighed against the risk of creating more dangerous pathogens."

Relman proposes that among those trying to suppress the lab-release hypothesis, there might have been "far too much protection of one's self and one's peers before allowing a really important question to receive a hearing." And scientists collaborating with researchers in China "might worry about their working relationship if they say anything other than 'This threat comes from nature.'" 

Other scientists say opposition to the lab-leak hypothesis was grounded more in a general disbelief that SARS-CoV-2 could have been deliberately engineered. "This is what became politicized," Perlman says. As to whether the virus may have escaped after evolving naturally, he says that is "more difficult to rule in or rule out."



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In an email message last week, Relman added that the question may never be fully settled. “From the natural-spillover angle, it would take a confirmed contact between a proven naturally infected host species (e.g., bat) and a human or humans who can be shown with reliable, confirmed time-and-place details to have become infected as a result of the encounter, ahead of any other known human cases,” Relman says, “and then shown to have passed on the infection to others.” As for the lab-leak scenario, there would need to be “confirmed evidence of possession of the virus ahead of the first cases, and a likely mechanism for escape into humans”—all of which become less likely with the passage of time. “Finding the possible immediate parents of SARS-CoV-2 would help to understand the recent genomic/evolutionary history of the virus,” he adds, “but not necessarily how and where that history occurred.”

As it stands now, pandemic preparedness faces two simultaneous fronts. On the one hand, the world has experienced numerous pandemic and epidemic outbreaks in the last 20 years, including SARS, chikungunya, H1N1, Middle East Respiratory Syndrome, several Ebola outbreaks, three outbreaks of norovirus, Zika, and now SARS-CoV-2. Speaking of coronaviruses, Ralph Baric, an epidemiologist at the University of North Carolina, Chapel Hill, says it’s “hard to imagine there aren’t variants” in bats with mortality rates approaching MERS’s 30% that also have “a transmissibility that is much more efficient.” He adds “That is



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four years,” he added, “and has announced plans to establish a network of hundreds of new BSL-3 and BSL-4 labs.”

Meanwhile, squabbles over SARS-CoV-2’s origins continue, some of them heated. During a recent exchange on Twitter, Chan was compared to a QAnon supporter and an insurrectionist. A few months prior, she had tweeted about issues of research integrity and stated that if the actions of scientists and journal editors were to obscure the origins of the virus, then those individuals would be complicit in the deaths of millions of people. (Chan has since deleted that tweet, which she says she regrets posting.)

“Temperatures are high,” Nielsen says, making it hard for qualified scientists to have any sort of serious discussion.

In Australia, Petrovsky says he is trying to stay above the fray. He says he was warned to avoid speaking publicly about his modeling findings. “A lot of people advised us, ‘Even if it’s good science, don’t talk about it. It will have a negative impact on your vaccine development. You will get attacked; they will try to discredit you.’” But in the end, that’s not what happened, says Petrovsky. Last year, amid the origins debate, his team became the first in the Southern Hemisphere to take a vaccine for covid-19 into human clinical trials.

“If we are at the point where all science is politicized and no one cares about truth and only being politically correct,” he says, “we may as well give up and shut down and stop doing science.”

Charles Schmidt is a recipient of the National Association of Science Writers’ Science in Society Journalism Award. His work has appeared in Science, Nature Biotechnology, Scientific American, Discover Magazine, and the Washington Post, among other publications.

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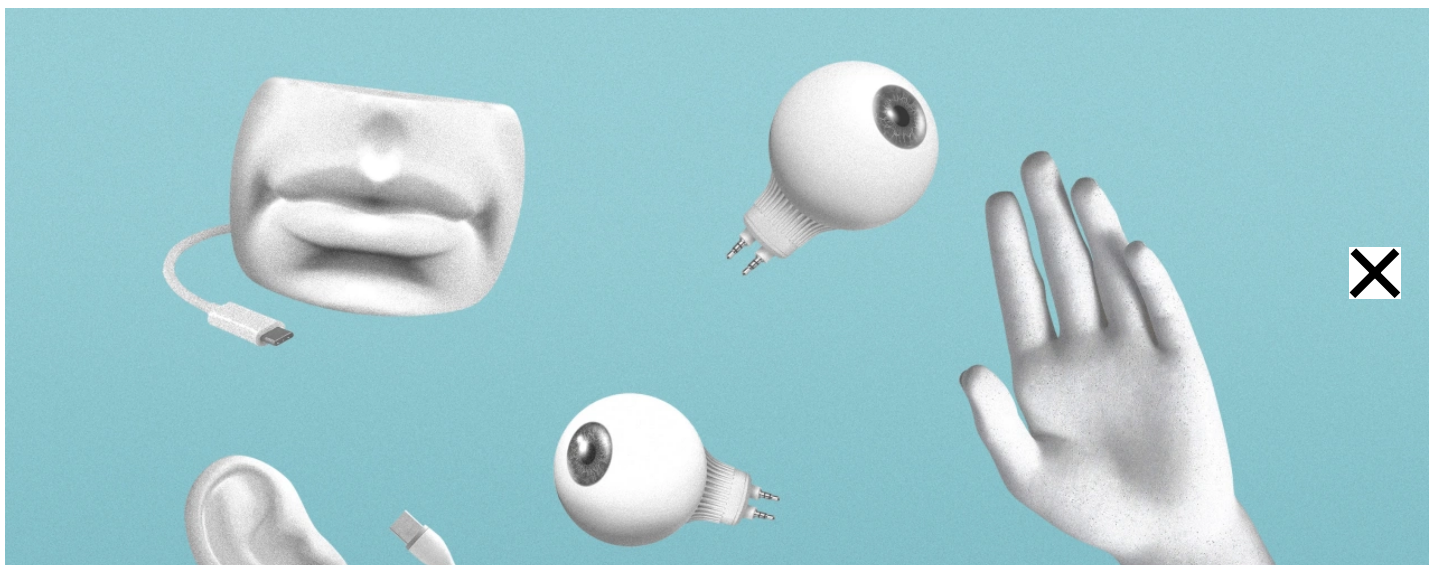
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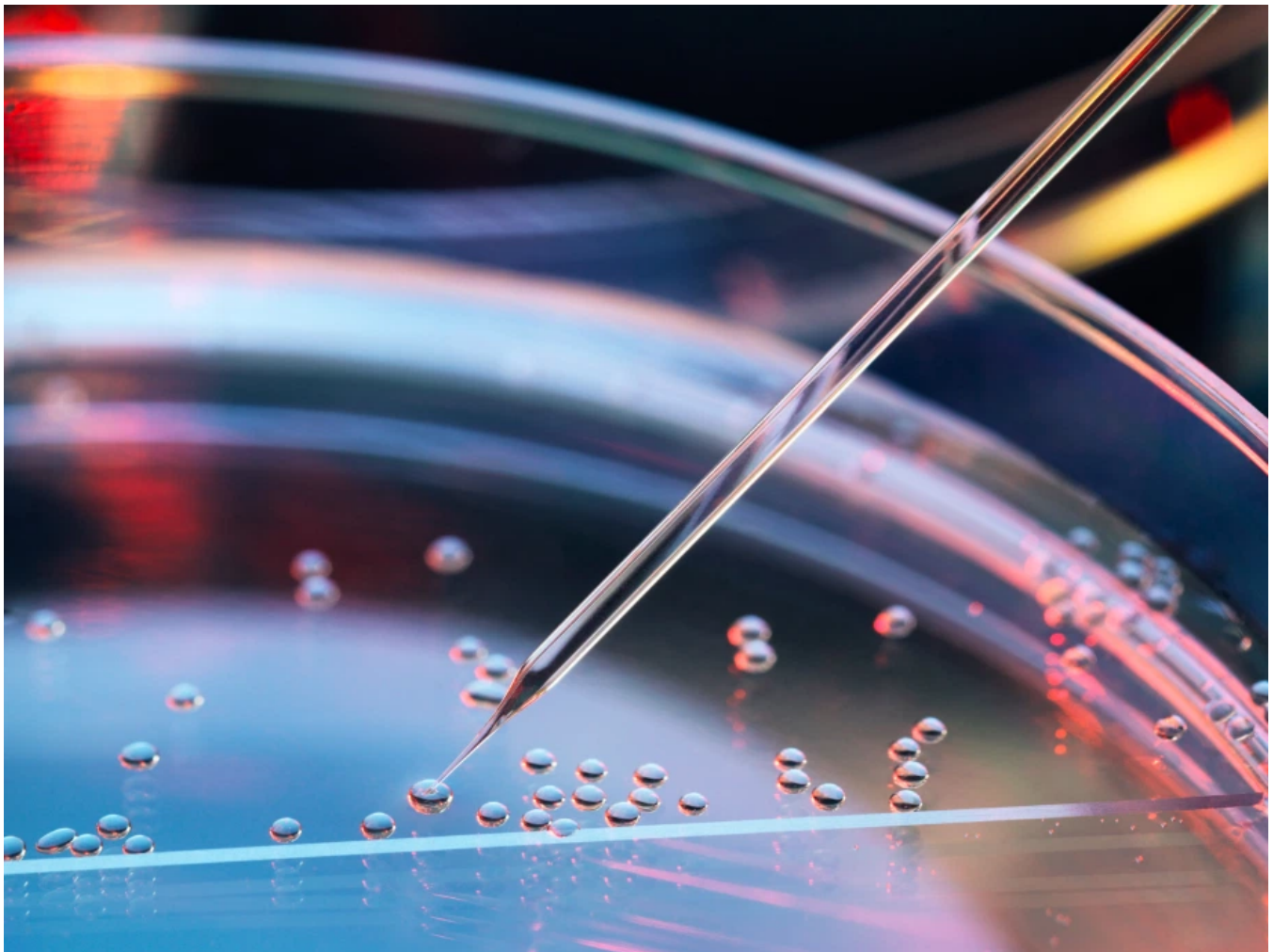
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